K092587

510(k) Summary
for
Bio-Rad Laboratories, Inc.
BioPlex® 2200 Rubella and CMV IgM

DEC - 3 2010

1. APPLICANT/SPONSOR

Bio-Rad Laboratories, Inc.
BioPlex Division
5500 East Second Street
Benicia, CA 94510

Contact Person: Juang Wang
Telephone: 510-741-4609

Date Prepared: November 30, 2010

2. DEVICE NAME

Proprietary Name: BioPlex® 2200 Rubella and CMV IgM Kit
BioPlex® 2200 Rubella and CMV IgM Calibrator Set
BioPlex® 2200 Rubella and CMV IgM Control Set

Common/Usual Name: Multi-Analyte Detection System for Rubella IgM and Cytomegalovirus (CMV) IgM

Classification Name:

Rubella virus serological reagents
Cytomegalovirus serological reagents
Calibrator, multi-analyte mixture
Single analyte controls, all kinds (assayed and unassayed)

3. PREDICATE DEVICES

- ADVIA Centaur® Rubella IgM K010668
- bioMeriéux VIDAS® CMV IgM K933549

4. DEVICE DESCRIPTION

The BioPlex® 2200 Rubella and CMV IgM kit uses multiplex flow immunoassay, a methodology that greatly resembles traditional EIA, but permits simultaneous detection and identification of many antibodies in a single tube. Rubella and CMV IgM test is to detect antibodies to Rubella and Cytomegalovirus (CMV).

Two (2) different populations of dyed beads are coated with cell lysates bearing Rubella or CMV antigens. The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel; the mixture is incubated at 37°C. After a wash cycle, anti-human IgM antibody, conjugated to phycoerythrin (PE), is added to the dyed beads, and this mixture is incubated at 37°C. The excess conjugate is removed in another wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of antibody captured by the antigen is determined by the fluorescence of the attached PE. Raw data are reported as relative fluorescence intensity (RFI).

Three additional dyed beads, an Internal Standard Bead (ISB), a Serum Verification Bead (SVB) and a Reagent Blank Bead (RBB) are present in each reaction mixture to verify detector response, the addition of serum or plasma to the reaction vessel and the absence of significant non-specific binding in serum or plasma.

The instrument is calibrated using a set of three (3) distinct serum based calibrators. A negative and CMV IgM calibrator is used to calibrate CMV assay, and a negative and rubella IgM calibrator is used to calibrate the rubella IgM assay. The cut-off value and assignment of the calibrators are determined by performing concordance and Receiver Operator Characteristic (ROC) analysis using the Centaur Rubella IgM and VIDAS CMV IgM predicate results as the standard. For Rubella and CMV, results of ≤ 0.8 AI are negative, 0.9 and 1.0 AI are equivocal and results of ≥ 1.1 AI are reported as positive.

The BioPlex 2200 Rubella and CMV IgM Control Set includes a negative control as well as a CMV IgM positive control and a Rubella IgM positive control. The BioPlex Rubella and CMV IgM Positive Controls are manufactured to give positive results, with values above the cut-off for each specific analyte. The BioPlex Rubella and CMV IgM Negative Control are manufactured to give negative results, with values below the cut-off for each specific analyte. The recommended frequency for performing quality control is once every 24-hour testing period. Performing quality control is also necessary after each new assay calibration and certain service procedures.

BioPlex® 2200 Rubella and CMV IgM Kit Components

The BioPlex 2200 Rubella and CMV IgM kit (665-1751) contains supplies sufficient for 100 tests.

Vial	Description
Bead Set	One (1) 10 mL vial containing two (2) different populations of dyed beads coated with lysates of Rubella and CMV; an Internal Standard Bead (ISB), a Serum Verification Bead (SVB) and a Reagent Blank Bead (RBB) in buffer with Glycerol and protein stabilizers (bovine). ProClin® 300 (0.3%) and sodium azide (<0.1%) as preservatives.
Conjugate	One (1) 5 mL vial, containing phycoerythrin-conjugated donkey polyclonal anti-human IgM antibody and phycoerythrin –conjugated murine monoclonal anti-human FXIII antibody, in buffer with stabilizers (bovine and equine).. ProClin® 300 (0.3%) , sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
Sample Diluent	One (1) 10 mL vial, containing goat anti-human IgG antibody and protein stabilizers (bovine and equine) in buffer. ProClin® 300 (0.3%) and sodium azide (<0.1%) as preservatives.

Additional Required Items, Available from Bio-Rad:

Catalog #	Description
663-1701	BioPlex 2200 Rubella and CMV IgM Calibrator Set: Three (3) 0.5 mL vials containing human IgM antibodies to Rubella and CMV, in a human serum matrix made from defibrinated plasma. All antibodies are derived from human disease state plasma. All calibrators contain ProClin® 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
663-1731	BioPlex 2200 Rubella and CMV IgM Control Set: Two (2) 1.5 mL Positive Control serum vials, containing human IgM antibodies to CMV; two (2) 1.5 mL Positive Control serum vials, containing human IgM antibodies to Rubella in a human serum matrix made from defibrinated plasma; and two (2) 1.5 mL Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All antibodies are derived from human disease state plasma. All controls contain Amikacin (0.003%), Cycloheximide ($C_{15}H_{23}NO_4$) (0.009%), Amphotericin B (0.002%), Cefotaxime Sodium (0.002%), Ciprofloxacin (0.005%), ProClin® 300 (≤0.3%), Sodium benzoate (≤0.1%) and sodium azide (<0.1%).
660-0817	BioPlex 2200 Sheath Fluid: Two (2) 4 L bottles containing Phosphate Buffered Saline (PBS). ProClin® 300 (0.03%) and sodium azide (<0.1%) as preservatives.
660-0818	BioPlex 2200 Wash Solution: One (1) 10 L bottle containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin® 300 (0.03%) and sodium azide (<0.1%) as preservatives.
660-0000	BioPlex 2200 Instrument and Software System.

5. INTENDED USE

BioPlex® 2200 Rubella and CMV IgM Kit

The BioPlex® 2200 Rubella and CMV IgM kit is a multiplex flow immunoassay intended for the qualitative detection of IgM antibodies to Rubella and Cytomegalovirus (CMV) in human serum and potassium EDTA or sodium heparin plasma.

The BioPlex 2200 Rubella and CMV IgM kit is intended for use with the Bio-Rad BioPlex 2200 System.

This kit is intended as an aid in the diagnosis of a current or recent Rubella and/or CMV infection, in individuals suspected of having one of the respective disease states including women of child bearing age.

This assay is not FDA cleared or approved for use in testing (screening) blood or plasma donors.

Performance characteristics for the Rubella and CMV IgM assays have not been evaluated in immunosupressed or organ transplant individuals. Performance characteristics of this kit have not been established for use in neonatal screening or for use at point of care facilities.

BioPlex® 2200 Rubella and CMV IgM Calibrator Set

The BioPlex 2200 Rubella and CMV IgM Calibrator Set is intended for calibration of the BioPlex 2200 Rubella and CMV IgM Reagent Pack.

BioPlex® 2200 Rubella and CMV IgM Control Set

The BioPlex 2200 Rubella and CMV IgM Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex Rubella and CMV IgM Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Rubella and CMV IgM Control Set has not been established with any other Rubella or Cytomegalovirus (CMV) IgM antibody assays.

6. Technological Characteristics and Substantial Equivalence

The following tables summarize the similarities and differences between the BioPlex 2200 Rubella and CMV IgM kit and the predicate devices used in comparative studies with the BioPlex 2200 Rubella and CMV IgM kit.

BioPlex® 2200 Rubella and CMV IgM Kit vs. Predicate Devices - Similarities

Item	BioPlex® 2200 Rubella and CMV IgM Kit	ADVIA Centaur Rubella IgM (K010668)	bioMeriéux, Inc. VIDAS® CMV IgM (K933549)
Intended Use	The BioPlex™ 2200 Rubella and CMV IgM kit is a multiplex flow immunoassay intended for the qualitative detection of IgM antibodies to Rubella, and Cytomegalovirus (CMV) in human serum and EDTA or heparinized plasma. The BioPlex™ 2200 Rubella and CMV IgM kit is intended for use with the Bio-Rad BioPlex 2200 System. This kit is intended as an aid in the diagnosis of a current or recent Rubella and/or CMV infection, in individuals suspected of having one of the respective disease states including women of child bearing age.	The ADVIA Centaur and ADVIA Centaur XP Rubella IgM assay is an IgM antibody capture microparticle direct chemiluminometric *in vitro* diagnostic immunoassay for the qualitative detection of IgM antibodies to the rubella virus in serum or plasma (EDTA, heparin) as an aid in the presumptive diagnosis of current or recent infection with rubella. WARNING: The calculated values for rubella IgM in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity.	VIDAS® CMV IgM (CMVM) assay is intended for use with a VIDAS (VITEK ImmunoDiagnostic Assay System) instrument as an automated enzyme-linked fluorescent immunoassay (ELFA) for the qualitative detection of anti-CMV IgM antibodies in human serum. It is intended to be used as an aid in the diagnosis of cytomegalovirus infection. It is not intended for use in testing (screening) blood or plasma donors.
Antigen	Partially purified cell lysates of Rubella, and CMV	Inactivated Rubella virus (HPV-77)	Purified and inactivated CMV antigen (Strain AD 169)
Assay Type	Qualitative detection for Rubella and CMV IgM	Same	Same
Analyte Detected	Human IgM antibodies to Rubella and CMV	Same	Same
Signal Detection	Fluorescence	-	Same
Matrices	Serum and plasma (EDTA and heparin)	Serum and plasma (EDTA and heparin)	-

BioPlex® 2200 Rubella and CMV IgM Kit vs. Predicate Devices - Differences

Item	BioPlex® 2200 Rubella and CMV IgM Kit	ADVIA Centaur Rubella IgM (K010668)	bioMeriéux, Inc. VIDAS® CMV IgM (K933549)
Number of Analytes Simultaneously Detected	Multiple (2)	Single	Single
Enzyme Conjugate	Phycoerythrin conjugated	Rubella antigen labeled with acridinium ester	Alkaline phosphatase conjugated
Matrices	Serum and plasma (EDTA and heparin)	-	Serum
Assay Technology	Multiplex flow immunoassay	Sandwich immunoassay using direct, chemiluminometric technology	Two-step enzyme immunoassay sandwich method with fluorescent detection (ELFA)
Signal Detection	Fluorescence	chemiluminesence	-
Solid Phase	Antigen-coated paramagnetic microbead reagent. Microbeads are infused with red and infrared fluorescent dyes for bead classification. Green fluorescence from the immunoassay label is used for analyte measurement.	anti-human IgM_{Fc} monoclonal antibody is covalently coupled to paramagnetic particles	Antigen-coated solid phase receptacles
Calibrator(s)	Multiple Calibrators	Single Calibrator	Single Calibrator
Controls	Negative Control and two separate Positive Controls for rubella and CMV IgM	Negative Control and Positive Control specific for rubella IgM	Negative Control and Positive Control specific for CMV IgM

7. PERFORMANCE TESTING

A series of studies was conducted to evaluate the performance of the BioPlex® 2200 Rubella and CMV IgM kit. The studies included reproducibility, interfering substances, cross-reactivity, expected values and method comparison. The results of all studies demonstrated that the BioPlex 2200 Rubella and CMV IgM kit performed according to its specifications.

A. Reproducibility

Separate internal and external reproducibility studies were conducted to evaluate the reproducibility of the BioPlex 2200 Rubella and CMV IgM kit on the BioPlex 2200 instrument. Reproducibility studies were based on the principles described in Clinical and Laboratory Standards Institute (CLSI) EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods.*

For the internal reproducibility study, three (3) panels made from serum and plasma (EDTA and heparinized) were assayed two (2) times in two (2) separate daily runs over 20 days (n=80).

The data were analyzed for within-run, between-run, between-day, and total precision and the standard deviation (SD) and percent coefficient of variation (% CV) were calculated.

The within-run precision for rubella IgM samples ranged from 4.3% to 5.5% in a serum matrix, 6.3% to 6.9% for EDTA and 4.8% to 9.5% for heparin plasma matrices. The within-run precision for CMV IgM samples ranged from 5.3% to 9.2% in a serum matrix, 4.9% to 11.8% for EDTA and 5.2% to 12.8% for heparin plasma matrices

The external reproducibility study was performed at three (3) clinical trial sites. Three lots of reagent packs, three lots of the BioPlex 2200 Rubella and CMV IgM Calibrator Set and three lots of BioPlex 2200 Rubella and CMV IgM Control Set were evaluated. Three (3) panels made from serum and plasma (EDTA and heparinized) were tested in quadruplicate over five (5) days (4 replicates x 1 run x 5 days x 3 testing sites = 60 replicates per panel member).

The data were analyzed for within-run, between-run, between-day, between-site, and total precision and the standard deviation (SD) and percent coefficient of variation (% CV) were calculated.

The within run precision for positive samples greater than or equal to the cut-off (≥ 1.1 AI) in all sample matrices ranged from 2.7% to 13.3% for Rubella IgM and

2.8% to 13.5% for CMV IgM. The total precision for positive samples greater than or equal to the cut-off (≥1.1 AI) ranged from 2.3% to 13.5% for Rubella IgM and 3.0% to 14.2% for CMV IgM.

B. Interfering Substances

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex 2200 Rubella and CMV IgM assays. The study was conducted based on the principles described in Clinical and Laboratory Standards Institute (CLSI) EP7-A2, *Interference Testing in Clinical Chemistry*. No interference was observed with any of the substances tested. The substances and the maximum levels tested are shown in the table below.

Interfering Substances

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin, Unconjugated	≤ 20 mg/dL
Bilirubin, Conjugated	≤ 30 mg/dL
Cholesterol	≤ 500 mg/dL
Red Blood Cells	≤ 0.4% (v/v)
Gamma Globulin	≤ 6 g/dL
Triglycerides	≤ 3300 mg/dL
Beta Carotene	≤ 0.6 mg/dL
Protein (total)	≤ 12 g/dL
Ascorbic Acid	≤ 3 mg/dL
Lithium Heparin	≤ 8000 units/dL
Sodium Heparin	≤ 8000 units/dL
EDTA	≤ 800 mg/dL
Sodium citrate	≤ 1000 mg/dL

C. Cross-Reactivity

A cross-reactivity study was performed to determine if samples from various disease states and other potentially cross-reacting agents interfere with test results when tested with the BioPlex 2200 Rubella and CMV IgM kit. Samples known to be positive for each of the potential cross-reactants, as determined by FDA cleared devices, were evaluated with the BioPlex 2200 Rubella and CMV IgM assay. All samples were pre-tested by the predicate devices and only those that tested negative by the predicate devices were further evaluated by the BioPlex 2200 Rubella and CMV IgG. The table below summarizes the number of samples scored negative by the BioPlex 2200 Rubella and CMV IgM assay within each of the cross-reactant panels. No significant cross reactivity was observed except for potential

cross reactivity of myeloma IgM samples tested with the rubella and CMV IgM assays, and EBV VCA and parvovirus B19 IgM and dsDNA samples tested with the CMV IgM assay.

Cross-Reactivity

Potential Cross-Reactant	BioPlex 2200 Rubella and CMV IgM Results			
	N	Rubella IgM	N	CMV IgM
ANA Screen	10	10	10	9
CMV IgM	10	10	0	N/A
dsDNA (SLE clinical)	10	10	10	9[b]
EBV VCA IgM	10	9	8	6
hCG (pregnancy)	10	10	10	10[a]
HIV IgG	10	10	10	10
HSV-1 or 2 IgM	9	8	10	10[b]
Hypergammaglobulinemia IgM	10	9	10	10
Influenza (compliment fixation)	10	10	10	10
Measles IgM	10	10	10	10
Mumps IgM	10	10	10	9
Myeloma IgM	9	7	7	5
Parvovirus B19 IgM	10	10[a]	9	4
Rheumatoid Factor (Total)	9	9	10	9[a]
Rubella IgM	0	N/A	10	10
T. gondii IgM	10	10	10	10
VZV IgM	10	10	10	10

a One BioPlex 2200 equivocal result
b Two BioPlex 2200 equivocal results
Note: The highlighted areas indicate that the potential cross reactivity with either Rubella or CMV IgM could not be ruled out.

D. IgM Detection

Rubella and CMV IgM-positive samples were selected and supplemented with matched specific IgG. The sample pools were split and further supplemented with dithiothreitol (DTT) which inactivates IgM activity. The samples were assayed neat and diluted into assay range in replicates of two. IgM was measured using Rubella and CMV IgM kit. The results are shown in below.

BioPlex 2200 Rubella and CMV IgM kit - Rubella IgM Specificity

Sample	Rubella IgM (AI) Before Treatment	DTT Treatment AI (% recovery)
Sample1	3.6	0.2 (5.6%)

Sample2	3.3	0.2 (6.1%)
Sample3	3	0.2 (6.7%)
Sample4	2.7	0.2 (7.4%)
Sample5	2.6	0.2 (7.7%)
Sample6	2.5	0.2 (8%)
Sample7	2.3	0.2 (8.7%)
Sample8	2.2	0.2 (9.1%)
Sample9	2.2	0.2 (9.1%)
Sample10	2.2	0.2 (9.1%)

BioPlex 2200 Rubella and CMV IgM kit - CMV IgM Specificity

Sample	CMV IgM (AI)* Before Treatment	DTT Treatment AI (% recovery)
Sample1	460	30.2 (6.6%)*
Sample2	341.5	26.4 (7.7%)*
Sample3	109	0.4 (0.4%)
Sample4	107	0.7 (0.7%)
Sample5	85.5	0.7 (0.8%)
Sample6	37.1	0.6 (1.6%)
Sample7	35.5	0.6 (1.7%)
Sample8	28.1	0.3 (1.1%)
Sample9	23.8	0.3 (1.3%)
Sample10	22.5	0.7 (3.1%)

*Values derived from dilution

E. Seroconversion Testing

Rubella IgM

Three Liquichek™ Rubella IgM seroconversion panels obtained from Bio-Rad Laboratories were tested with the BioPlex 2200 Rubella and CMV IgM kit. The results shown in below were compared to a commercial method.

Panel RP001	Rubella IgM	
Day	Commercial Method Index	BioPlex 2200 Rubella and CMV IgM kit AI
0	0.20 (Neg)	0.3 (Neg)
2	0.10 (Neg)	0.2 (Neg)
7	0.15 (Neg)	0.2 (Neg)
9	0.00 (Neg)	0.2 (Neg)
14	0.29 (Neg)	0.3 (Neg)

17	0.91 (Eq)	1.1 (Pos)
21	9.57 (Pos)	>4.0 (Pos)
24	7.95 (Pos)	>4.0 (Pos)
28	1.87 (Pos)	1.9 (Pos)
31	4.92 (Pos)	3.7 (Pos)
35	7.31 (Pos)	3.1 (Pos)
38	3.54 (Pos)	1.8 (Pos)
42	2.43 (Pos)	1.7 (Pos)
45	1.83 (Pos)	1.3 (Pos)
50	1.95 (Pos)	1.2 (Pos)

The BioPlex 2200 Rubella and CMV IgM test detected Rubella IgM four days earlier demonstrating greater sensitivity.

Panel RP011	Rubella IgM	
Day	Commercial Method Index	BioPlex 2200 Rubella and CMV IgM kit AI
0	0.21 (Neg)	0.2 (Neg)
3	0.00 (Neg)	0.2 (Neg)
9	0.02 (Neg)	0.2 (Neg)
12	0.00 (Neg)	0.2 (Neg)
16	**1.64 (Pos)**	**1.1 (Pos)**
19	5.94 (Pos)	>4.0 (Pos)
24	8.95 (Pos)	>4.0 (Pos)
27	7.69 (Pos)	>4.0 (Pos)
31	4.50 (Pos)	3.7 (Pos)
36	2.70 (Pos)	2.4 (Pos)
39	1.78 (Pos)	1.8 (Pos)
43	1.12 (Pos)	1.2 (Pos)
46	**0.77 (Neg)**	**0.8 (Neg)**
50	0.43 (Neg)	0.8 (Neg)
53	0.32 (Neg)	0.6 (Neg)
57	0.32 (Neg)	0.6 (Neg)
60	0.13 (Neg)	0.4 (Neg)
64	0.37 (Neg)	0.5 (Neg)
67	0.00 (Neg)	0.4 (Neg)
71	0.00 (Neg)	0.5 (Neg)

The BioPlex 2200 Rubella and CMV IgM test showed comparable performance to a commercial method.

Panel RP014	Rubella IgM	
Day	Commercial Method Index	BioPlex 2200 Rubella and CMV IgM kit AI
0	0.00 (Neg)	<0.2 (Neg)
5	0.00 (Neg)	<0.2 (Neg)
7	0.00 (Neg)	<0.2 (Neg)

12	0.00 (Neg)	<0.2 (Neg)
14	0.23 (Neg)	0.7 (Neg)
19	**2.44 (Pos)**	**2.3 (Pos)**
21	2.55 (Pos)	2.4 (Pos)
26	2.58 (Pos)	2.2 (Pos)
28	2.15 (Pos)	1.8 (Pos)
33	1.5 (Pos)	1.6 (Pos)
35	1.5 (Pos)	1.2 (Pos)
40	1.00 (Pos)	**1.0 (Eq)**
42	**0.76 (Neg)**	0.8 (Neg)

The BioPlex 2200 Rubella and CMV IgM test showed comparable performance to a commercial method, except for the day 40 sample which scored equivocal in the BioPlex 2200 Rubella and CMV IgM test and positive (at the cutoff) in the comparison test.

CMV IgM

Bio-Rad Laboratories Liquichek™ CMV IgM Seroconversion panel was assayed with BioPlex 2200 Rubella and CMV IgM kits and a commercial method. The results are shown in below. The BioPlex 2200 Rubella and CMV IgM test was able to detect CMV IgM in all the samples compared to a commercial test which scored equivocal at 59 days.

Panel RP003	CMV IgM	
Day	Commercial Methos Index	BioPlex 2200 Rubella and CMV IgM kit AI
1	1.16 (Pos)	>4.0 (Pos)
4	1.62 (Pos)	>4.0 (Pos)
8	2.44 (Pos)	>4.0 (Pos)
51	1.16 (Pos)	3.4 (Pos)
55	1.04 (Pos)	3.0 (Pos)
59	0.84 (Eq)	2.1 (Pos)
65	0.85 (Eq)	2.3 (Pos)
67	0.75 (Eq)	2.0 (Pos)
72	0.68 (Neg)	1.7 (Pos)
74	0.62 (Neg)	1.5 (Pos)
79	0.64 (Neg)	1.8 (Pos)
84	0.54 (Neg)	1.7 (Pos)
88	0.72 (Eq)	2.1 (Pos)
95	0.59 (Neg)	1.7 (Pos)
99	0.65 (Neg)	1.6 (Pos)

F. Expected Values

The observed prevalence for the Rubella and CMV IgM using the BioPlex 2200 Rubella and CMV IgM assay was determined using samples submitted for Rubella (300, US) or CMV IgM (400; 300 US +100 Europe) testing. The results are presented in the tables below. The predictive values of the test are dependent on the prevalence. As rubella incidence decreases, the predicative positive value of rubella IgM results decreases.

Note: Each laboratory should establish frequency distributions for their specific patient populations.

Expected values using the BioPlex 2200 Rubella and CMV IgM kit in test ordered population

Age	Gender	Rubella IgM (US)		CMV IgM (US)		CMV IgM (EU)	
		Pos/Total	% Prevalence	Pos/Total	% Prevalence	Pos/Total	% Prevalence
0 - 10	F	0/13	0.0%	0/4	0.0%	0/0	N/A
	M	0/11	0.0%	0/6	0.0%	0/2	0.0%
11 - 20	F	0/44	0.0%	1/19	5.3%	0/4	0.0%
	M	0/12	0.0%	0/20	0.0%	0/1	0.0%
21 - 30	F	4/80	5.0%	1/41	2.4%	1/36	2.8%
	M	0/8	0.0%	0/10	0.0%	0/2	0.0%
31 - 40	F	4/55	7.3%	1/34	2.9%	3/42	7.1%
	M	0/8	0.0%	3/17	17.6%	0/1	0.0%
41 - 50	F	3/26	11.5%	1/35	2.9%	0/6	0.0%
	M	1/12	8.3%	0/19	0.0%	0/2	0.0%
51 - 60	F	0/19	0.0%	1/23	4.3%	0/1	0.0%
	M	0/9	0.0%	1/33	0.0%	0/1	0.0%
61 - 70	F	0/1	0.0%	0/16	0.0%	0/1	0.0%
	M	0/1	0.0%	0/14	0.0%	0/0	N/A
71 +	F	0/0	N/A	0/2	0.0%	0/0	N/A
	M	0/1	0.0%	0/7	0.0%	0/1	0.0%
Total		12/300*	4.0%**	9/300	3.0%	4/100	4.0%

*One of pregnant women (N=71) was Rubella IgM positive.
,**Since 2001, the incidence of Rubella in the US has been less than 10/1,000,000 population.

G. Method Comparison

Performance of the BioPlex 2200 Rubella and CMV IgM kit was evaluated against corresponding commercially available Rubella and CMV kits. Three clinical sites tested 700 prospective samples submitted for: Rubella (300 - U.S.), and CMV IgM testing (400;300 U.S. + 100 Europe). Of the 300 samples submitted for Rubella IgM testing, 71 females were pregnant women. Results are shown in the table below:

Of the 300 clinical ordered samples test for Rubella IgM, the positive percent agreement was 66.7% and the negative percent agreement was 95.6%.

Of the 71 clinical ordered pregnancy samples test for Rubella IgM, the negative percent agreement was 96.8%.

Of the 400 clinical ordered samples tested for CMV IgM, the positive percent agreement was 53.8% and the negative percent agreement was 97.7%.

The results are presented in the table below.

Method Comparison: Prospective Study

Test Ordered				BioPlex 2200 Rubella and CMV IgM kit					
				Pos (+)	Eqv	Neg (-)	Total	Pos (+) % Agreement	Neg (-) % Agreement
Commercially Available Immunoassay	Rubella IgM	Test Ordered	Pos (+)	2	0	1	3	66.7% (2/3) 95% CI 20.8 – 93.9%	95.6% (282/295) 95% CI 92.6 – 97.4%
			Eqv	0	2	0	2		
			Neg (-)	10	3	282	295		
			Total	12	5	283	300		
		Pregnant Women*	Pos (+)	0	0	0	0	N/A	96.8% (70/71) 95%CI 92.8% - 99.8%
			Eqv	0	0	0	0		
			Neg (-)	1	0	70	71		
			Total	1	0	70	71		
	CMV IgM	Test Ordered	Pos (+)	7[a]	0	3[a]	10	53.8% (7/13)	97.7% (377/386)

			Eqv	1	1	3	5	
			Neg (-)	5[b]	3	377[a]	385	
			Total	13	4	383	400	

a. One sample that was equivocal by the predicate device was adjudicated by two out of three FDA cleared devices.
b. Two samples that were equivocal by the predicate device was adjudicated by two out of three FDA cleared devices.
** Pregnant women is the subset of the test ordered population.*

Comparative Testing: Retrospective Study

Performance of the Rubella and CMV IgM kit was evaluated against corresponding commercially available Rubella and CMV IgM immunoassays. Three clinical sites tested 107 Rubella (45 females with 89% in 15-45 age group, 49 males and 13 with unknown gender) and 229 CMV (144 females with 84% in 15-45 age group and 85 males) presumptive IgM positive samples.. Positive samples for Rubella and CMV IgM were selected by another FDA cleared test and the respective commercially available immunoassays used for the comparative analysis. The results are presented in the table below.

Characteristics of Samples with Presumptive Positive Status

Presumptive Positive for Rubella or CMV IgM			BioPlex Rubella and CMV IgM kit				
			Pos(+)	Eqv	Neg(-)	Total	Pos(+) % Agreement
Commercially Available Immunoassay	Rubella IgM	Pos(+)	103	1	3	107	96.3%
		Eqv	0	0	0	0	(103/107)
		Neg(-)	0	0	0	0	95% CI
		Total	103	1	3	107	90.3 – 98.5%
	CMV IgM	Pos(+)	209[a]	3	17[b]	229	91.3%
		Eqv	0	0	0	0	(209/229)
		Neg(-)	0	0	0	0	95% CI
		Total	209	3	17	229	86.9 – 94.3%

a. One sample that was equivocal by the predicate device was adjudicated by two out of three FDA cleared devices.

b.Two samples that were equivocal by the predicate device was adjudicated by two out of three FDA cleared devices.

Matrix Comparison

Matched serum and plasma (potassium EDTA and sodium heparin) samples drawn from 20 individual donors were acquired from commercial sources. All samples were evaluated in replicates of 10. Mean plasma AI values were compared to matched mean serum AI values. Scatter plots comparing the performance of serum samples against potassium EDTA and sodium heparin plasma samples along with the corresponding slopes of regression and correlation coefficient (r) are shown in below. All assays pass the slope specification of 1.0 ± 0.2, intercepts specification of ± 0.2, and correlation coefficient (r) of ≥ 0.98.

Figure 1. Rubella IgM: EDTA vs. Serum (N=20)

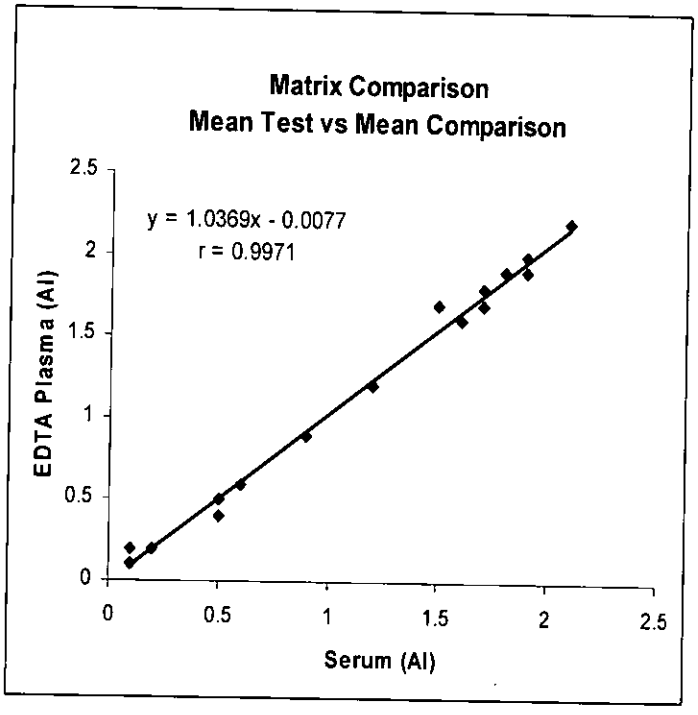


Figure 2. Rubella IgM: Heparin vs. Serum (N=20)

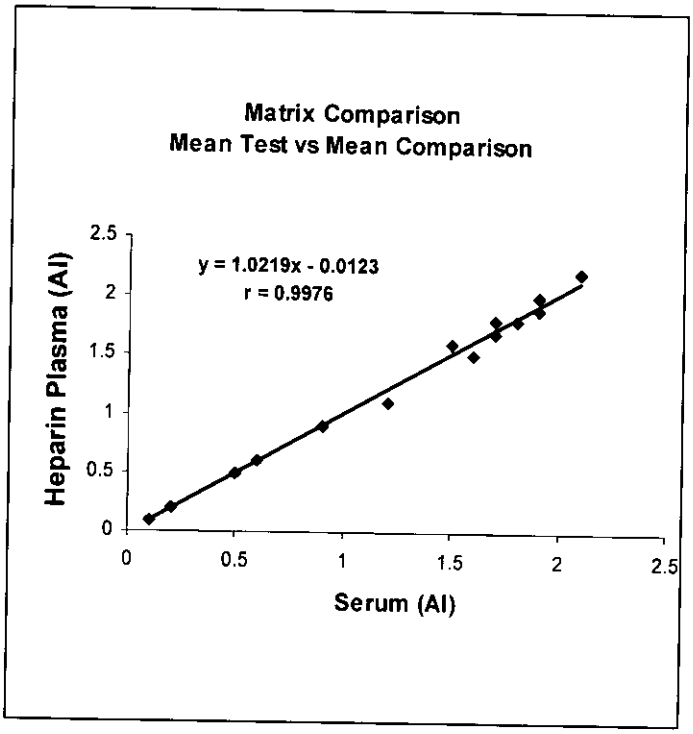


Figure 3. CMV IgM: EDTA vs. Serum (N=20)

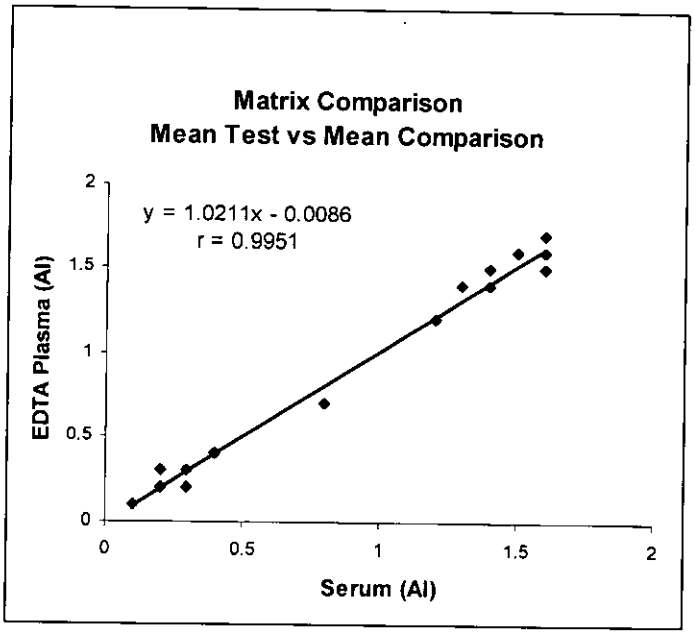
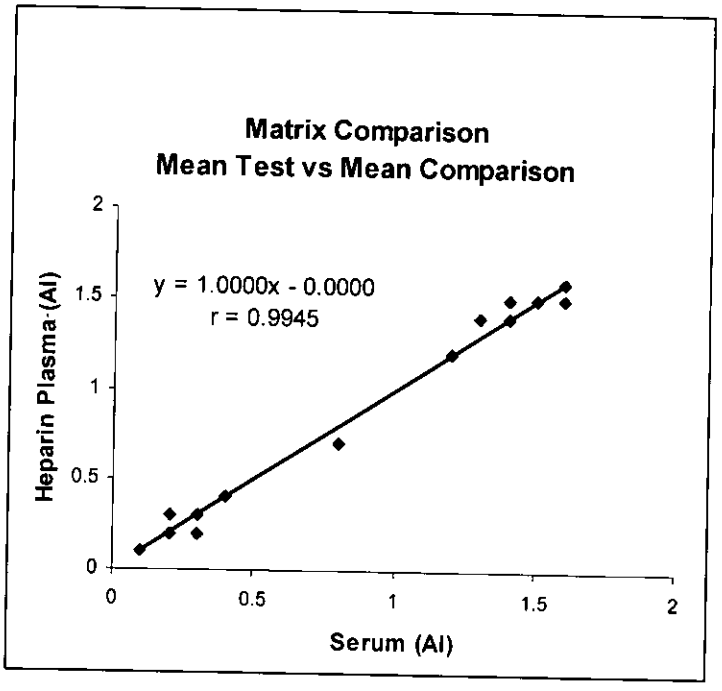


Figure 4. CMV IgM: Heparin vs. Serum (N=20)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Bio- Rad Laboratories, Inc.
BioPlex 2200 Division
c/o Juang Wang
Regulatory Affairs Representative
5500 East Second Street
Benicia, CA 94510

DEC - 3 2010

Re: K092587
Trade/Device Name: BioPlex® 2200 Rubella and CMV IgM Kit on the BioPlex® 2200 Multi Analyte Detection System
Regulation Number: 21CFR§866.3510
Regulation Name: Rubella Virus Serological Reagents
Regulatory Class: Class II
Product Code: LFX, LKQ, LFZ, JIX, JJX
Dated: November 30, 2010
Received: December 1, 2010

Dear Mr. Wang:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication(s) for use

DEC - 3 2010

510(k) Number (if known): k092587

Device Name: BioPlex® 2200 Rubella and CMV IgM Kit on the BioPlex® 2200 Multi Analyte Detection System
BioPlex® 2200 Rubella and CMV IgM Calibrator Set
BioPlex® 2200 Rubella and CMV IgM Control Set

Indications for Use:

The BioPlex® 2200 Rubella and CMV IgM kit

The BioPlex® 2200 Rubella and CMV IgM kit is a multiplex flow immunoassay intended for the qualitative detection of IgM antibodies to Rubella and Cytomegalovirus (CMV) in human serum and potassium EDTA or sodium heparin plasma.

The BioPlex 2200 Rubella and CMV IgM kit is intended for use with the Bio-Rad BioPlex 2200 System.

This kit is intended as an aid in the diagnosis of a current or recent Rubella and/or CMV infection, in individuals suspected of having one of the respective disease states including women of child bearing age.

This assay is not FDA cleared or approved for use in testing (screening) blood or plasma donors.

Performance characteristics for the Rubella and CMV IgM assays have not been evaluated in immunosupressed or organ transplant individuals. Performance characteristics of this kit have not been established for use in neonatal screening or for use at point of care facilities.

BioPlex® 2200 Rubella and CMV IgM Calibrator Set

The BioPlex® 2200 Rubella and CMV IgM Calibrator Set is intended for the calibration of the BioPlex® 2200 Rubella and CMV IgM Reagent Pack.

BioPlex® 2200 Rubella and CMV IgM Control Set

The BioPlex® 2200 Rubella and CMV IgM Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 instrument and BioPlex 2200 Rubella and CMV IgM Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Rubella and CMV IgM Control Set has not been established with any other Rubella and CMV IgM assays.

Prescription Use __X___ AND/OR Over-the-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(Please do not write below this line-Continue on another page if needed)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) k092587